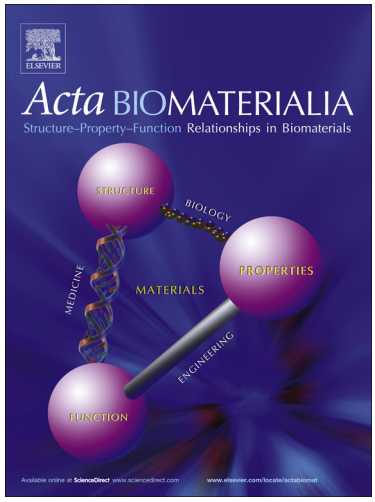

Bioluminescent and micro-computed tomography imaging of bone repair induced by fibrin-binding growth factors

Olaia F Vila, Mikaël M Martino, Laura Nebuloni, Gisela Kuhn, Soledad Pérez-Amodio, Ralph Müller, Jeffrey A Hubbell, Nuria Rubio, Jerónimo Blanco

PII: S1742-7061(14)00240-2
DOI: http://dx.doi.org/10.1016/j.actbio.2014.05.028
Reference: ACTBIO 3250

To appear in: *Acta Biomaterialia*

Received Date: 5 February 2014
Revised Date: 6 May 2014
Accepted Date: 23 May 2014

Please cite this article as: Vila, O.F., Martino, M.M., Nebuloni, L., Kuhn, G., Pérez-Amodio, S., Müller, R., Hubbell, J.A., Rubio, N., Blanco, J., Bioluminescent and micro-computed tomography imaging of bone repair induced by fibrin-binding growth factors, *Acta Biomaterialia* (2014), doi: http://dx.doi.org/10.1016/j.actbio.2014.05.028

Bioluminescent and micro-computed tomography imaging of bone repair induced by fibrin-binding growth factors

Olaia F Vila[1,2], Mikaël M Martino[3], Laura Nebuloni[4], Gisela Kuhn[4],Soledad Pérez-Amodio[2,5], Ralph Müller[4], Jeffrey A Hubbell[3], Nuria Rubio[1,2], Jerónimo Blanco[1,2,*].

[1] *Catalonian Institute for Advanced Chemistry (IQAC-CSIC), Barcelona, Spain*

[2] *Networking Research Center on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Spain*

[3]*Institute of Bioengineering, École Polytechnique Fédérale de Lausanne (EPFL), 1015 Switzerland*

[4]*Institute for Biomechanics, Eidgenössische Technische Hochschule Zürich (ETZH), 8093 Switzerland*

[5]*Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain.*

**Corresponding author Jeronimo.Blanco@iqac.csic.es*

In this work we have evaluated the capacity of BMP-2 and fibrin-binding PDGF-BB to support cell growth and induce bone regeneration using two different imaging technologies to improve understanding of structural and organizational processes participating in tissue repair. Human mesenchymal stem cells from adipose tissue (hAMSCs) expressing two luciferase genes, one under the control of the CMV promoter and the other under the control of a tissue-specific promoter (osteocalcin or PECAM), were seeded in fibrin matrices containing BMP-2 and fibrin-binding PDGF-BB, and further implanted intramuscularly or in a mouse calvarial defect. Then, cell growth and bone regeneration were monitored by bioluminescence imaging (BLI) to analyze the evolution of target gene expression, indicative of cell differentiation towards the osteoblastic and endothelial lineages. Non-invasive imaging was supplemented with micro-computed tomography (microCT) to evaluate bone regeneration and high-resolution microCT of vascular casts. Results from BLI showed hAMSC growth during the first week in all cases, followed by a rapid decrease in cell number; as well as an increment of osteocalcin but not PECAM-1 expression 3 weeks after implantation. Results from microCT show that the delivery of BMP-2 and PDGF-BB by fibrin induced the formation of more bone and improves vascularization, resulting in more abundant and thicker vessels, in comparison with controls. Although inclusion of hAMSCs in the fibrin matrices made no significant difference in any of